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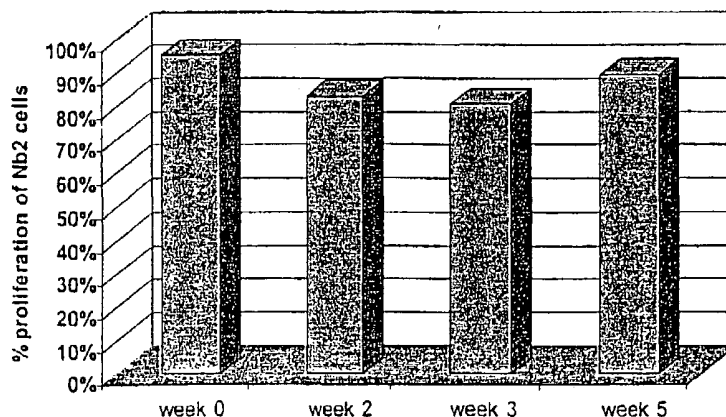
[Continued on next page]

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(75) Inventors/Applicants (for US only): **ROSEN, Craig, A.** [US/US]; 22400 Rolling Hill Lane, Laytonsville, MD

(54) Title: **ALBUMIN FUSION PROTEINS**

Stability of HA-hGH at 37°C in cell culture media



2ng/ml HA-hGH

hGH has no activity by week 2

(57) Abstract: The present invention encompasses albumin fusion proteins. Nucleic acid molecules encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Additionally the present invention encompasses pharmaceutical compositions comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/31794

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A01N 37/18; A61K 38/00

US CL : 530/350, 362; 514/2

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350, 362; 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 6,210,901 B1 (SEIDEL et al.) 03 April 2001 (03.04.2001), column 2, lines 1-8).	1-12 ----- 13, 14, 17, 18, 20
X --- Y	US 6,121,231 A (PETIT et al.) 19 September 2000 (19.09.2000), column 16, lines 13-20 and 65-67; and column 17 lines 1-9.	1-14, 20 ----- 17-19
X, E	US 6,548,653 B1 (YOUNG et al.) 15 April 2003 (15.04.2003), column 1, lines 14-28; column 15, lines 9-22; claims 1- 20.	1-14, 17-20
X	US 5,216,131 A (LASKY et al.) 01 June 1993 (01.06.1993), column 7, lines 21-47; column 10, lines 57-60.	1-14 and 17-20
X,P	US 2001/0056075 A1 (GYURIS et al.) 27 December 2001 (27.12.2001), claim 1, 4, 15, 16, , 26; whole document.	1-12, 17-20

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

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"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

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albumin conjugated proteins may reduce the need to formulate protein solutions with large excesses of carrier proteins (such as albumin, unfused) to prevent loss of Therapeutic proteins due to factors such as binding to the container.

[0008] The present invention encompasses albumin fusion proteins comprising a Therapeutic protein (e.g., a polypeptide, antibody, or peptide, or fragments and variants thereof) fused to albumin or a fragment (portion) or variant of albumin. The present invention also encompasses albumin fusion proteins comprising a Therapeutic protein (e.g., a polypeptide, antibody, or peptide, or fragments and variants thereof) fused to albumin or a fragment (portion) or variant of albumin, that is sufficient to prolong the shelf life of the Therapeutic protein, and/or stabilize the Therapeutic protein and/or its activity in solution (or in a pharmaceutical composition) *in vitro* and/or *in vivo*. Nucleic acid molecules encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells.

[0009] The invention also encompasses pharmaceutical formulations comprising an albumin fusion protein of the invention and a pharmaceutically acceptable diluent or carrier. Such formulations may be in a kit or container. Such kit or container may be packaged with instructions pertaining to the extended shelf life of the Therapeutic protein. Such formulations may be used in methods of treating, preventing, ameliorating or diagnosing a disease or disease symptom in a patient, preferably a mammal, most preferably a human, comprising the step of administering the pharmaceutical formulation to the patient.

[0010] In other embodiments, the present invention encompasses methods of preventing treating, or ameliorating a disease or disorder. In preferred embodiments, the present invention encompasses a method of treating a disease or disorder listed in the "Preferred Indication Y" column of Table 1 comprising administering to a patient in which such treatment, prevention or amelioration is desired an albumin fusion protein of the invention that comprises a Therapeutic protein portion corresponding to a Therapeutic protein (or fragment or variant thereof) disclosed in the "Therapeutic Protein X" column of Table 1 (in the same row as the disease or disorder to be treated is listed in the "Preferred Indication Y" column of Table 1) in an amount effective to treat prevent or ameliorate the

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           580                  585

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           20                  25                  30  
 Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu  
           35                  40                  45  
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           50                  55                  60  
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   65                  70                  75                  80  
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           85                  90                  95  
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          100                 105                 110  
 Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His  
          115                 120                 125  
 Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg  
   130                 135                 140  
 Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg  
  145                 150                 155                 160  
 Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala  
          165                 170                 175  
 Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser  
          180                 185                 190  
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          195                 200                 205  
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 Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp  
          245                 250                 255  
 Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser  
   260                 265                 270  
 Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His  
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 Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser

290	295	300
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Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr 340 345 350		
Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu 355 360 365		
Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro 370 375 380		
Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu 385 390 395 400		
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Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys 420 425 430		
Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys 435 440 445		
Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His 450 455 460		
Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser 465 470 475 480		
Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr 485 490 495		
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp 500 505 510		
Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala 515 520 525		
Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu 530 535 540		
Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys 545 550 555 560		
Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val 565 570 575		
Ala Ala Ser Gln Ala Ala Leu Gly Leu 580 585		

&lt;210&gt; 19

&lt;211&gt; 57

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;221&gt; primer\_bind

<223> primer used to generate XhoI and ClaI  
site in pPPC0006